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## Association Between G308A Polymorphism of TNF- $\alpha$ Gene and TNF- $\alpha$ levels, Insulin Resistance and Histological Alterations in Patients with NAFLD

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### Abstract

**Introduction:** Tumor necrosis factor alpha (TNF- $\alpha$ ) has been linked to the pathophysiology of non-alcoholic fatty liver disease (NAFLD).

**Objective:** To examine the impact of the TNF- $\alpha$  gene's G308A polymorphism on TNF- $\alpha$  levels as well as the histological alterations and insulin resistance (IR) associated with NAFLD.

**Methods:** This was a cross-sectional study that included 76 NAFLD patients. For every patient, a biopsy is done in order to confirm the NAFLD. In order to predict IR scores (homeostatic model assessment [HOMA]), we assessed clinical and anthropometric features as well as carried out biochemical tests (insulin, glucose, total cholesterol, low-density lipoprotein cholesterol, and triglycerides). TNF- $\alpha$  plasma levels and the G308A polymorphism of the TNF- $\alpha$  gene were examined together.

**Results:** 57 patients (75.0%) had the G308G genotype (wild group), while eighteen patients (7 females and 12 males) (25.0%) had the G308A genotype (mutant group). Compared to patients with the wild genotype (22.6%), patients in the mutant group had moderate-to-severe portal inflammation (81.2%) in the liver biopsy. Compared to the wild group (62.7%), the mutant group exhibited higher levels of moderate-to-severe fibrosis (68.2%). With the dependent variable (fibrosis) controlled for age, sex, BMI, and genotype, the multivariable analysis revealed that HOMA remained in the model, with an increase in HOMA levels, there was an increase in the probability of developing fibrosis OR 2.16; 95% CI (1.86-2.48) and moderate-to-severe inflammation OR 0.97; 95% CI (0.65-1.29).

**Conclusion:** Compared to the wild group, patients with the mutant genotype are more likely to develop moderate-to-severe portal inflammation and fibrosis.

### Keywords:

Tumor necrosis factor alpha; non-alcoholic fatty liver disease; insulin resistance; G308A polymorphism; TNF- $\alpha$  gene.

### Abbreviations:

Tumor necrosis factor alpha (TNF- $\alpha$ ); non-alcoholic fatty liver disease (NAFLD); insulin resistance (IR); homeostatic model assessment (HOMA).

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